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19. (Amended) A pharmaceutical composition [according to claim 18, wherein said] comprising a pharmaceutical carrier and as an active ingredient, an effective amount of a dibenz[b,e]oxepin compound [is] defined in claim 6.

REMARKS

Claim 1 has been amended in order to more particularly recite the present invention, Claims 2 and 19 have been amended so as to utilize formats in better conformance with accepted U.S. practice and Claims 3, 5-10 and 13-17 have been amended to delete that subject which is recited within Claim 1. Additionally, Claims 11 and 12 have been cancelled as reciting non-selected or cancelled species.

The Examiner has required that Applicants formally elect a single species for the purposes of search, to which species the claims shall be restricted if no generic claim is found to be allowable. Applicants' representative previously selected compound No. 20 and such selection is hereby affirmed.

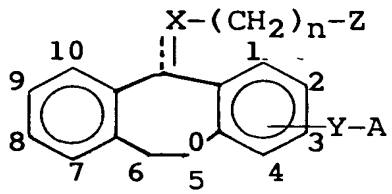
Claims 1-4, 18 and 19 stand rejected as being improper Markush claims since the definition of the bridge group X recites structures said to be so structurally diverse and patentably distinct that a reference anticipating one would not be a reference against the

others under Section 103. In response, Claim 1 has been amended to recite that X is =CH-, pursuant to the Examiner's suggestion and accordingly, withdrawal of these rejections is earnestly solicited.

Claim 19 stands rejected under 35 U.S.C. § 112 as indefinite for failing to particularly point out and distinctly claim the subject matter of the present invention. Specifically, the Examiner states that Claim 19 is improperly dependent upon both of Claims 6 and 18. In response, Claim 19 has been amended so as to expressly recite the desired subject matter of Claim 18 and therefore, now depends only from Claim 6. Accordingly, this rejection is also believed to be overcome and Applicants respectfully request that it be withdrawn.

Claims 1-11 and 13-19 stand rejected under 35 U.S.C. § 103 as obvious over U.S. Patents Nos. 3,354,155 (Tretter) or 3,420,851 (Bloom), in view of 4,585,788 (Helsley), each newly cited, or U.S. Patents Nos. 4,282,365 (Rokach), 4,396,550, 4,465,835 or 4,596,804 (each to Takizawa) or the J. Med. Chem. (Vol. 19, No. 7, Vol. 20, No. 11, or Vol. 21, No. 7) articles, each previously of record. These rejection are respectfully traversed.

The present invention relates, in pertinent part, to a dibenz[b,e]oxepin compound of the formula:



wherein X is =CH- and A is carboxyl, lower alkoxy carboxyl, -CONHOH or $-CONR_1R_2$, i.e., carboxyl groups and specific derivatives thereof. In other words, the present invention requires both an 11-position aminoalkylidene and a carboxyl or carboxyl derivative substituted for a hydrogen bound to a benzene nucleus. These features are neither taught nor suggested by the cited art.

Tretter and Bloom both teach that 11-aminopropylidene substituted dibenzoxepines are useful as psychotherapeutic agents and have spasmolytic activity, and Bloom also teaches that certain psychotherapeutic agents may also exhibit antihistaminic activity. However, neither reference teaches or suggests the carboxyl or carboxyl derivative substituents bound to the benzene nucleus, as is required by the present invention.

Nor are these deficiencies remedied by the secondary references. Rather, Rokach, Helsley and the J. Med. Chem. articles (Vols. 19-21) only teach a carboxyl and derivatives thereof as substituents bound to the benzene nucleus. Such compounds are said to exhibit antiallergic (Rokach) or antiinflammatory (Helsley and J.

Med. Chem.) activities. However, these references do not teach or suggest Applicants' 11-position aminoalkylidene. Rather, they only teach the use of an 11-position carbonyl or methylene (or equivalents thereof).

Finally, the Takizawa patents which teach an 11-position aminoalkyleneamino do not teach or suggest the aminoalkylidene group of the present invention. Thus, Applicants respectfully suggest that the pending Claims recite unobvious and patentable subject matter.

However, in order to even better reduce the issues and further distinguish the present invention from the prior art, Applicants have enclosed herewith a Declaration under Rule 132, comparing the present invention to such art. As the Examiner will appreciate, for the best clarification of the record, the Declaration not only compares the compounds of the primary references (e.g., Tretter and Bloom), but also the appropriate compounds of the secondary references as well. The Declaration is executed by Kenji Ohmori who is, of course, an inventor of this application.

As illustrated in Table 1, Compounds A (Tretter's Example VI) and B (Bloom's 11th compound of Example X) exhibit more than ten-fold worse anti PCA (antiallergic) activity, while providing immeasurably worse M_1 binding (receptor affinity, an indication of expected side effects) activity than the analogous compounds of the present invention.

Similarly, in Table II, Compounds C (Compound No. 2, J. Med. Chem., Vol. 19; Compound No. 7, J. Med. Chem., Vol. 20) and D (reference example 8) both provide at least 100-fold worse antiallergic activities than the compounds of the present invention.

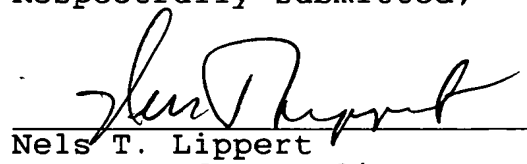
Finally, even regarding Takizawa, the data in Declaration Table III illustrates that the present invention is again unexpectedly superior. In fact, the present invention provides 10-fold superior allergic activity results (anti PCA) over the prior art therein.

Accordingly, it is clear that Applicants' compounds having both an 11-position amino alkylidene group and a carboxyl group or carboxyl group derivative substituent provides both unexpectedly high antiallergic activities and moreover, fewer deleterious side effects than the closest compounds of the prior art. These advantages are, of course, in no manner suggested by such art.

Claims 1-10 and 13-19 remain in prosecution.

In view of the above amendments and remarks, and the accompanying Declaration, reconsideration and allowance of this application are earnestly solicited.

Respectfully submitted,



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